

Exhibit 6

Abstract

Hirano *et al.*, Proc Natl Acad Sci, 80:46-50 (1983)



PubMed Nucleotide Protein Genome Structure PMC Taxonomy OMIM Bc

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Isolation of genomic DNA clones spanning the entire fibronectin gene.

Hirano H, Yamada Y, Sullivan M, de Crombrughe B, Pastan I, Yamada KM.

Overlapping recombinant clones that appear to encompass the entire fibronectin gene have been isolated by step-wise screening of a library of chicken genomic DNA fragments. The first genomic clone was isolated by using a cloned fibronectin cDNA hybridization probe. The remaining clones were obtained by using defined fragments of this and successive genomic clones as probes. Their relationships and overlaps were determined by electron microscopy, restriction mapping, and heteroduplex analysis. Based on electron microscopic analysis of hybrids between these clones and fibronectin mRNA, the gene is approximately 48 kilobases long, more than 5 times larger than the corresponding mRNA. This large gene contains at least 48 exons interrupted by introns of highly variable size. The total exon size as estimated by R-loop analysis is 8 kilobases, similar to the mRNA for fibronectin. With the exception of the 3'- and 5'-terminal exons, the exons are small and roughly similar in size. The average exon size is 147 +/- 37 base pairs, corresponding to a protein unit of 50 amino acids. The nucleotide sequence of one of these exons was determined. The deduced amino acid sequence has marked homologies with one type of repetitive protein sequence unit known to exist in bovine fibronectin. These results suggest that the gene for fibronectin may have arisen by multiple gene duplications of a primordial gene or genes approximately equal to 150 base pairs long.

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